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Relationship between orientation to a blast and pressure wave propagation inside the rat brain

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ABSTRACT

Exposure to a blast wave generated during an explosion may result in brain damage and related neurological impairments. Several mechanisms by which the primary blast wave can damage the brain have been proposed, including: (1) a direct effect of the shock wave on the brain causing tissue damage by skull flexure and propagation of stress and shear forces; and (2) an indirect transfer of kinetic energy from the blast, through large blood vessels and cerebrospinal fluid (CSF), to the central nervous system. To address a basic question related to the mechanisms of blast brain injury, pressure was measured inside the brains of rats exposed to a low level of blast (~35 kPa), while positioned in three different orientations with respect to the primary blast wave; head facing blast, right side exposed to blast and head facing away from blast. Data show different patterns and durations of the pressure traces inside the brain, depending on the rat orientation to blast. Frontal exposures (head facing blast) resulted in pressure traces of higher amplitude and longer duration, suggesting direct transmission and reflection of the pressure inside the brain (dynamic pressure transfer). The pattern of the pressure wave inside the brain in the head facing away from blast exposures assumes contribution of the static pressure, similar to hydrodynamic pressure to the pressure wave inside the brain.

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1. Introduction

The symptoms of brain injury in combatants are often attributed to post-traumatic stress disorder (PTSD) (Hoge et al., 2008). However, it has been suggested that in many cases exposure to primary blast wave, blast overpressure (BOP) results in manifestations of traumatic brain injury (TBI) (Okie, 2005; Ling et al., 2009). Neurologists are concerned that at least 30% of military personnel who have engaged in active combat for four months or longer in Iraq or Afghanistan are at risk of potentially disabling neurological disorders from BOP, all without suffering a scratch (Glasser, 2007). There is a growing understanding that blast brain injuries are very different from those caused by penetrating or skull-fracture trauma (Cernak and Noble-Haeusslein, 2010). Several mechanisms by which primary blast wave can damage the brain have been proposed, including: (1) mechanical displacement of brain resulting in contusions and hemorrhages and direct transmission of the shock wave to the brain in the form of stress and shear forces resulting in diffuse axonal injuries (Taber et al., 2006); and (2) indirect transfer of kinetic energy from the blast through large blood vessels and cerebrospinal fluid (CSF) to the central nervous system resulting in intracerebral hemorrhages as predominant lesions (Cernak et al., 2001). The role(s) of these different mechanisms in the process of brain damage are not known. The lack of understanding the mechanisms of primary blast brain damage may have serious consequences such as: (1) absence of tolerance curves for primary blast TBI (bTBI), i.e. the relationship between brain injury and mechanical conditions (blast overpressure); and (2) absence of sufficient and effective design of protective equipment that would reduce blast load to the brain. Recently, it was suggested that measuring brain biomechanical responses such as pressure, linear/angular acceleration, force and torque, inside the brain could provide the link between load and physiological injury and is vital for understanding the mechanisms of brain injury after blast (Desmoulin and Dionne, 2009).

To address a basic question related to the mechanisms of blast brain injury, we made point-pressure measurements inside the cerebral ventricles of rats exposed to a low level of blast (~35 kPa) in three different orientations (i.e., head facing blast, right side exposed to blast and head facing away from blast) with respect to the blast wave propagation. We hypothesized that the contribution of direct transfer of pressure to the brain should be predominant in the head facing blast (head-on) position, while indirect transfer should be prevalent in the side-on (one side exposed to blast) orientation. We also exposed animals in the head facing away from blast orientation inside and outside of PVC tubing, which was used as a

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14. ABSTRACT

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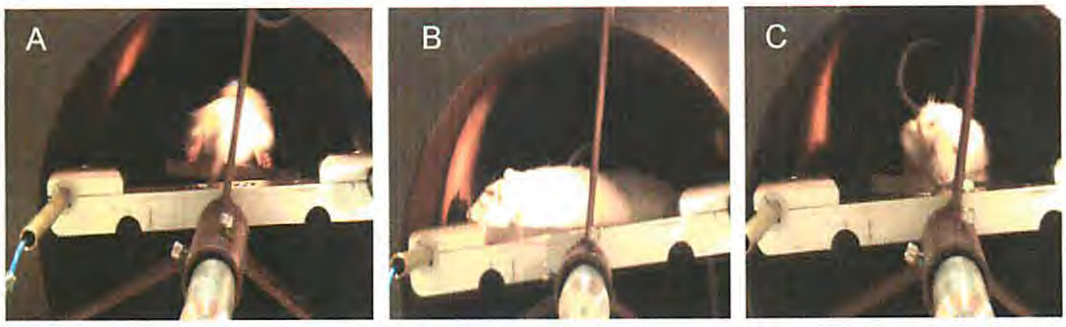

Fig. 1. Orientation of animals exposed to blast. Animals were placed inside the shock tube in: (A) frontal, head-on position, with the head facing the blast wave; (B) lateral, side-on position with the right side of body exposed to blast; (C) backward position with the head facing away from blast.

shield to examine how the pressure wave is propagated inside the body. We interpret intra-cerebral pressure measurements as surrogates of the actual and putative mechanisms of injury triggered by exposure to BOP.

2. Materials and methods

2.1. Animal preparation and exposure to blast

Male Sprague–Dawley rats (250–300 g) were anesthetized with ketamine/xylazine (i.p. 60/5 mg/kg) and immobilized in a stereotaxic frame. An incision was made longitudinally along the dorsal midline of the head and the skin retracted to visualize bregma and lambda. A 1 mm hole was drilled for a guide cannula using a tapered dental burr at 0.9 mm posterior from bregma and 1.5 mm lateral to midline. Two small sterile stainless steel screws anchored the guide cannula in the cranium. A guide cannula (0.8 mm O.D.) was inserted through the hole 3.5 mm below the skull surface to reach the lateral cerebral ventricle (Paxinos and Watson, 1986). A dummy cannula (a wire) was left in the guide cannula until exposure to BOP. Cranioplastic cement was applied to fix the cannula and screws to the skull. The surgical wound was closed with Vetabond surgical glue, and if necessary, one or two sutures (Chavko et al., 2007).

The next day animals were anesthetized again (ketamine/xylazine, i.p.) and exposed to blast. To restrict body movement from the blast impact and prevent subsequent secondary blast injuries, animals were secured into a holder placed 30 cm inside the compressed air-driven shock tube with Mylar membranes rupturing at predetermined pressure thresholds (Elsayed, 1997). Animals were subjected to blast with a mean peak overpressure of 36 ± 2 kPa in three different positions: (1) frontal, a head-on orientation with the head facing blast; (2) side-on orientation, with the right side exposed to blast; and (3) in a backward position to blast with the head facing away from blast (Fig. 1). Animal orientation to blast was randomized using the MINITAB statistical software package. After exposure, the animals were sacrificed and the cannula position in the ventricle was confirmed after an injection of dye (methylene blue).

In another experiment, animals were placed inside the PVC tubing (dimensions of the tubing: length 22 cm; O.D. 8.9 cm, wall thickness 0.6 cm) to differentiate between direct transfer of blast pressure (head facing blast) and propagation of the pressure wave inside the body (head facing away from blast) to the pressure level inside the brain. Animals were placed inside the PVC tubing that was either closed at both ends, or only at the front end (Fig. 4) or exposed to blast.

2.2. Blast pressure measurement

Pressure wave inside the brain, was measured by a microfiber pressure sensor (Samba AB, Västra Frölunda, Sweden). A pressure transducer, consisting of a silicon sensor chip (0.36 mm diameter) attached to the tip of an optical fiber (0.25 mm diameter), was inserted into the guide cannula placed in lateral ventricle and connected to a SAMBA 3000 Monitor operating at 40 kHz sampling rate.

Simultaneously, the reference pressure outside the animal was measured by two piezoelectric (PCB) sensors placed between the rat head and the shock tube walls (one sensor on each side) approx 3 cm from the head and 5 cm from the wall (PCB Piezotronics, Buffalo, NY). One sensor was aligned parallel to the direction of propagation of the BOP and measured a static flow pressure while the other gauge was aligned perpendicular to the blast flow to measure reflected and dynamic pressure. Signals were recorded by the NI data acquisition system (National Instrument, Austin, TX) at a sampling rate of 500 kHz.

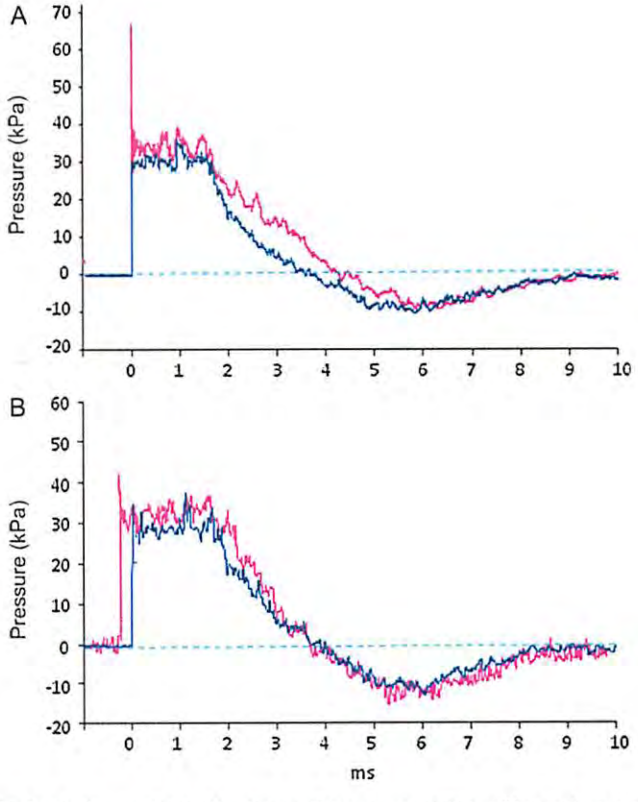

Fig. 2. Shock wave detected by: (A) two PCB sensors and (B) two fiber optic sensors, aligned parallel (blue lines) or perpendicular (red lines) to the direction of the blast flow. Delay in response between fiber optic sensors is caused by the more proximal position of the face-on sensor. The signal was recorded simultaneously with all four sensors.

3. Results

During the first part of this study we measured some basic characteristics of the blast wave produced inside the shock tube. Fig. 2A shows the blast wave recorded by two PCB sensors to measure side-on (static) and face-on (reflected) pressures inside the shock tube. The wave manifests a typical pattern consisting of a positive overpressure followed by a negative under-pressure then return to ambient pressure. A plateau pressure ~35 kPa measured by the dynamic probe, was approximately 5–10% higher than the static probe overpressure measurement. Observed shockwaves can deviate somewhat from the ideal normal shocks governed by ideal Rankine–Hugoniot relations (Kinney and Graham, 1985) due to the superposition of internal reflections of the shockwaves and other factors such as rupture of the diaphragm. The plateau pressure following the pressure wave front is characteristic for a specific shock tube and depends on the ratio between expansion and compression chambers as well as the overall dimensions of the shock tube. The behavior of each test is highly predictable as the tube has a stable and reproducible performance. On the other hand, the shockwaves generated by explosives are related to the state of the exothermic chemical reactions and are more complex with very high velocities that follow decay similar to that of the classical Friedlander's equation (sharp impulsive raise in pressure followed by exponential decay in pressure). In the case of IEDs, typical free field pattern is distorted by the geometry of the environment where the event takes place (Iremonger, 1997).

The pressure wave inside the shock tube was also measured with miniature fiber optic pressure sensors and compared with the PCB sensor pressure characteristics (Fig. 2B). The microfiber sensor placed in a face-on position detected a lower reflected pressure spike than the spike measured with the PCB probe, however a plateau pressure level and duration of the wave was comparable with the face-on PCB probe. The difference can be caused from lower sampling rate 40 kHz for microfiber sensor compared with 500 kHz at PCB sensors or by their specific characteristics. The pressure level and duration of the wave were comparable with the PCB probes placed parallel or perpendicular to the direction of the blast wave.

Some differences associated with orientation to the blast were observed in the pressure wave curves (Fig. 3). Pressure wave tracings at the head-on position had higher amplitudes, faster rise times and longer durations than the tracings at either side-on or head facing away positions. The pressure wave in the head facing away from blast orientation was about the same amplitude as in the side-on orientation; however, it had shorter durations and longer rise times. In all orientations, the rise times of the intracerebral pressure wave were slower than the rise times observed in air (Table 1).

The detection of the pressure wave in brains of animals exposed in the head facing away from blast orientation could be caused by the pressure wave propagation through the body or from the outside static pressure flow. To differentiate between the two mechanisms, the pressure wave was measured in brains of rats placed inside plastic PVC tubing and exposed to blast. When rats were placed inside the tube closed at both ends (Fig. 4A), no pressure waves were detected inside the brain indicating that the tube provides an effective shield against pressure wave transmission. The pressure wave in brains of animals exposed inside the tube with both ends open was similar to the one observed in brains of animals exposed without the PVC tubing (Fig. 4B). When animals were positioned in the front of PVC tubing (head facing the blast wave) with the tube closed at the front end, a slow rising pressure wave with depressed amplitude was still detected inside the brain (Fig. 4C). Finally, in animals positioned in the back PVC tubing (head facing away from blast) with the tubing closed at the front end, a narrow pressure wave was detected inside the brain (Fig. 4 D).

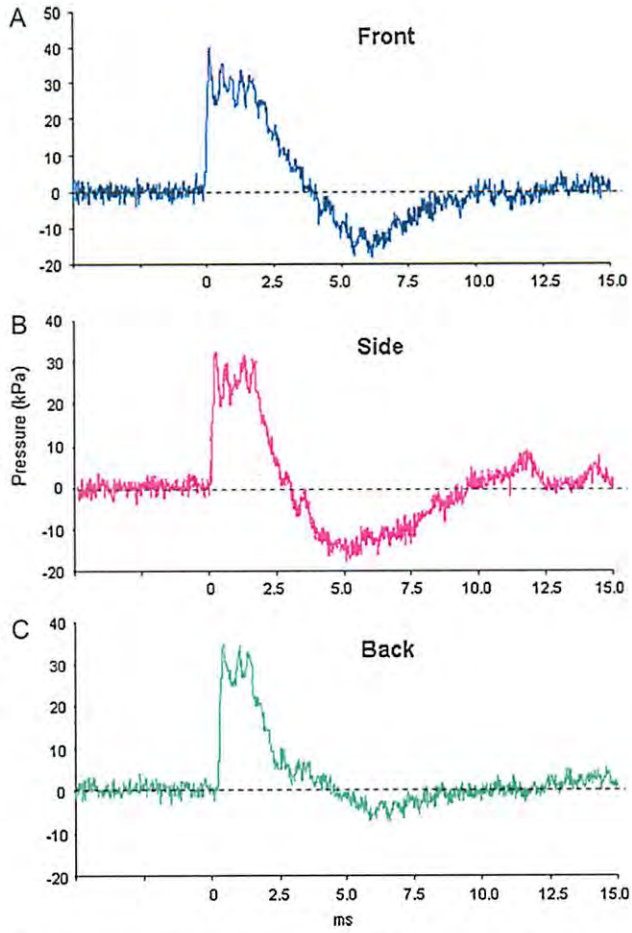

Fig. 3. Representative pictures of pressure wave in the brain of one animal exposed to blast in three different orientations: (A) head-on (head facing the blast wave); (B) side-on (right side of body exposed to blast); (C) backward to blast (head facing away from blast).

Table 1
Basic characteristics of the pressure wave inside rat brain exposed to blast in three different orientations.

Orientation	Peak overpressure (kPa)	Rise time (ms)	Overpressure duration (ms)
Air	36.5 ± 1.6	0.07 ± 0.42	4.1 ± 0.3
Head facing blast	41.5 ± 1.7*	0.19 ± 0.04*	4.1 ± 0.2
Right Side facing blast	33.6 ± 3.2#	0.26 ± 0.02*,#	3.3 ± 0.1*,#
Head facing away from blast	36.3 ± 2.0#	0.31 ± 0.02*,#	2.9 ± 0.4*,#

Values are means from 5 different exposures ±SD. Pressure wave in air was measured by microfiber sensor placed outside exposed animals.
* $P<0.05$ compared with air.
# $P<0.05$ compared with the head facing blast (frontal) exposure.

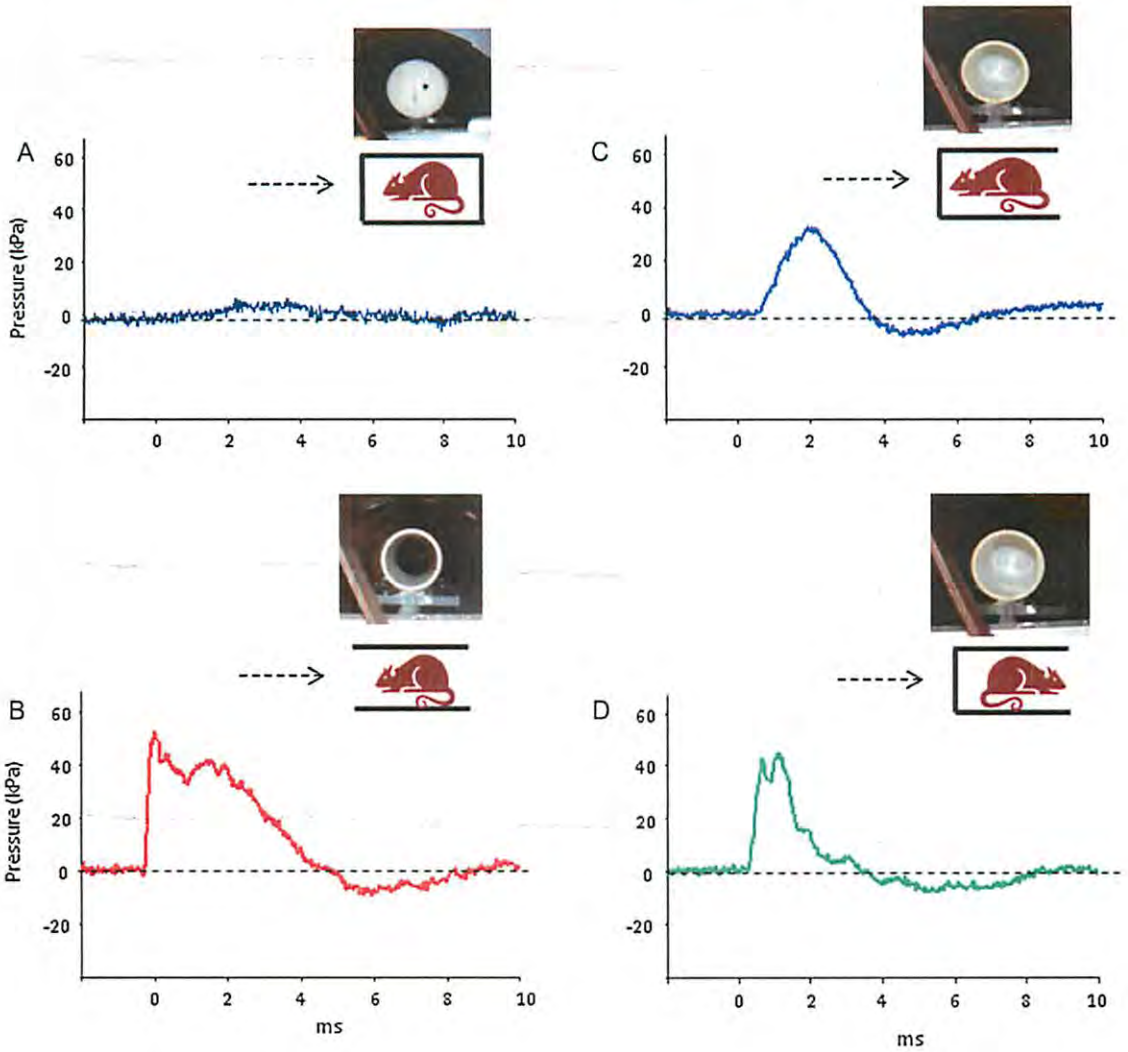

Fig. 4. Pressure wave measured in the brain of animal placed inside the PVC plastic tubing: (A) rat, head-on orientation inside the closed PVC tube; (B) rat, head-on orientation inside the open PVC tube; (C) rat, head-on inside the PVC tubing with only the front end closed; (D) rat, head facing away from blast inside the PVC tubing with the front end closed.Shown are positions of rats inside the PVC tubing relative to direction of blast (arrows).

4. Discussion

TBI has become the "signature wound" of the current conflicts in Iraq and Afghanistan due to the increased use of improvised explosive devices (IEDs) (Ling et al., 2009). It has become more evident that the primary pressure wave from a detonated IED can initiate functional, biochemical and morphological alterations in the brain without the signs characteristic for other types of traumatic injuries, such as those caused by penetration/fragmentation (Cernak et al., 1996).

Recently, it was shown that the skull imposes little protection against propagation of the pressure wave inside the brain (Chavko et al., 2007; Säljö et al., 2008). A still unresolved controversy is how primary blast forces injure the brain and whether the final damage results from multiple pathways of energy transfer. Several mechanisms have been suggested, namely: (1) direct interaction of the pressure wave with the skull and its subsequent propagation through the brain (Moss et al., 2009); and (2) transfer of kinetic energy from the blast wave through the vascular system and CSF (Cernak et al., 2001). The contribution(s) of these pathways transferring energy to the brain and their roles in blast brain injury is not known. The understanding of basic mechanisms of blast brain injury would have some practical implications for the protection of troops in the field which presents several challenges. Paradoxically, due to improved body armor and more efficient thoracic protection, combat personnel are surviving injuries that previously would have been lethal; however, this survival has increased the incidence of brain injuries from primary blast wave (Martin et al., 2008). This suggests the possibility that either: (a) soldiers wearing protection are emboldened to get closer to the center of explosion thereby exposed to higher blast levels (Mellor and Cooper, 1989); or (b) Kevlar vests may actually facilitate brain damage by increasing intrathoracic pressure (Young et al., 1985). Another concern related to personal protection is that even blast-resistant helmets do not effectively protect the skull against brain injury. Without solid knowledge of blast injury mechanism(s) or standardized mechanical surrogates, the effectiveness of blast protective equipment remains in question (Desmoulin and Dionne, 2009).

We assumed that the contribution of direct versus indirect transfer of pressures to brain damage would differ depending on the orientation to the blast and the surface area directly exposed to blast. It could be reasonable to assume that the direct impact to the head should be higher in exposures with the head facing the blast wave while the indirect transfer of pressure should be more significant in exposures involving orientation with the one side exposed to the blast wave (compressing both the chest and

abdomen). In parallel, it can be also assumed that different orientation(s) to the blast wave would result in different types of brain damage, e.g. more brain contusions and epidural hemorrhages after the direct impact of blast to the head (head facing the blast wave) compared with the mechanism(s) of indirect pressure transfer (side-on exposure to blast) producing predominantly intraparenchymal hemorrhages.

The blast wave is often characterized by blast overpressure that usually refers to the static, freely flowing pressure, measurable by a pencil-shaped probe with a sensor parallel to the propagation of the blast. Obviously, the static pressure can contribute to the pressure measured inside the tissues; however, it is not explicitly the loading force on the target, especially not in the frontal, the head facing blast orientation. Fig. 2 illustrates that the probe placed perpendicular to the blast direction measured an approximately 10% higher pressure level than the probe positioned parallel to the blast propagation. In addition, reflected pressure wave(s) had a slower decline and longer duration. The difference between these two measurements is a measure of kinetic energy, known as dynamic pressure in the blast wave (Benzinger et al., 2009). Our data suggests that the frontal exposure resulted in higher amplitudes and longer durations of the pressure waves in the brain compared with the side-on exposed animals. The head facing away from blast exposure produced a narrow pressure wave in the brain with amplitudes comparable to those observed with the side exposure to blast. In fact, pressure amplitudes measured in frontal, head-on orientation were about 10% higher when compared with peak external shock wave pressures, in accordance with the data published for deceased rhesus monkeys (Romba and Martin, 1961) and anesthetized rabbits (Clemedson, 1956).

Comparisons of in vivo measurements in three orientations with respect to the pressure amplitude and duration suggests that the brain is most impacted by shock waves in frontal exposures, which is in agreement with the direct hit assumption. Simulated experiments using finite element hydrocode demonstrated that a blast wave causes the skull to dynamically deform, and that this flexure creates localized regions of large and low pressures throughout the brain (Moss et al., 2009). Even modest skull flexures from a non-lethal blast can produce sufficient skull flexures and damaging effects even without a head impact. It could be supposed that the skull flexures could be different in different orientations to blast, with the highest impact and higher pressure at the head-on orientation to blast. Another factor for the observed differences involves the placement of the probe in the brain in relation to the distance from the skull; only 3 mm from the skull at the head-on position, compared to 6 mm at the side-on orientation.

Results show that even in exposures in the backward orientation (head facing away from blast) a significant pressure can be measured inside the brain. The pressure wave amplitudes in the head facing away from blast exposures were comparable with the side-on exposures, but the pressure wave durations were much shorter. Because there is a low direct impact of the blast to head, it could be assumed that the pressure inside the brain in the head facing away from blast orientation is caused mainly by the static pressure, and contribution of dynamic impact is minimal. One analogy could be made with the hydrodynamic pressure forces originated from water flow pressing on a solid surface. Another possibility is that the pressure inside brain at the head facing away from blast exposure is caused by the pressure wave propagation all the way through the body to brain.

To discriminate between different possibilities regarding how the shock wave reaches the brain in head facing away from blast orientation, animals were exposed inside the PVC tubing with either the front end or both ends of the PVC tubing closed. When both ends of the tube were closed there was no pressure wave detected inside the tube, indicating that pressure cannot enter the tube through the PVC tubing. However, pressure was still measured inside the brain in both head facing and head facing away from blast orientations, when only the front end of the PVC tube was closed. The pressure wave characteristics in the brain in head facing away orientation were similar to the wave measured outside the PVC tubing. This suggests that: (1) the propagation of pressure through the body does not contribute significantly to the pressure inside brain at the head facing away orientation, and (2) even more perplexing, pressure can diffract and propagate into open objects oriented opposite to the blast wave propagation. This possibility was validated by computational analysis in identical experimental setting by Dr. A. Przekwas (CFDR Huntsville, AL, personal communication).

The data, at least with the respect to the pressure wave amplitude and duration, indicate that the contribution of direct pressure propagation to brain is likely more significant than the contribution of indirect pressure transfer (head-on, versus side-on exposed animals). However, this does not exclude the possibility that indirect pressure transfer could contribute to the pressure level and brain damage in the side-on exposures as it was suggested by a lower degree of brain damage in animals protected against blast by Kevlar vests (Long et al., 2009). The degree of this contribution, if any, needs to be determined. So far, there is no evidence of circulatory system involvement in brain damage after blast and recent modeling data indicates that small hemorrhages (petechia) observed after blast exposure in some deep brain areas are the result of local pressurization rather than fluid pressure transmission (Leung et al., 2008). More conclusive findings about the contribution of indirect pressure wave transfer to the brain would require additional experiments examining the effects of head and whole body protection on the pressure propagation in the brain.

Our results in rats and results by others in pigs (Säljö et al., 2008) suggest that the rat brain might be extremely sensitive to blast injury, as only a small part of a blast wave is absorbed by the skull and brain parenchyma before reaching subcortical structures. The shape of a pressure wave inside the brain compared to air indicates differences in velocity of the wave propagation, likely a result of reflection from boundaries between tissues of different densities. This may represent a critical factor for neuronal damage as it appears that the pressure integrated over time, constitutes a key factor for altering biophysical properties of the membranes rather than the peak pressure amplitude (Kodama et al., 2000).

Some considerations from the present experiments can relate to head protection offered by helmets. Current equipments tend to be optimized for impact or ballistic head protection with little or no consideration for blast mitigation and/or protection against it. It appears from simulated blast modeling that the clearance gaps between the helmet and head allow the blast wave to wash under the helmet to pressure levels exceeding those outside the helmet (Moss et al., 2009). Without padding, the pressure impacts directly on the skull. Padding decreases pressure impact to the skull; however, it increases the mechanical load in the brain coupled with the helmet motion (Moss et al., 2009). Moreover, it appears that pressure could penetrate under the helmet not only when the head is facing blast, but actually from any direction, even from the side opposite the direction of the explosion (Bardi, 2008). Moreover, the flow of pressure from front and back could combine and produce substantially greater pressure. It appears from both, the Moss study and the present study that effective head protection would require a new helmet design that would deflect blast wave energies, eliminate gaps and prevent access of pressure from all angles under the helmet. Our results also demonstrated that because of the blast wave diffraction, subjects are not completely protected against the blast wave even when taking cover behind large objects obstructing the direction of the blast.

In conclusion, the pattern(s) of the pressure wave inside the brain have indicated higher pressure wave amplitude at the head

facing blast compared with the head facing away from blast and with the side-on exposures. This may suggests the higher contribution of the direct transfer of pressure than indirect pressure transfer to the brain after blast. The pressure measured inside the brain in the head facing away from blast orientation implies contribution of both, the dynamic pressure and static pressure (similar to hydrodynamic pressure) to the pressure wave inside the brain. Pressure wave diffraction could be a significant source of pressure inside the body as under the certain conditions blast waves can change their direction and can propagate under the gaps in protective armors and helmets from any angles and orientations.

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